UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,765	09/30/2003	Hoa Duc Nguyen		6272

7590 03/27/2008

HIGH STANDARD PRODUCTS CORPORATION
SUITE 225
14441 BEACH BLVD.
WESTMINSTER, CA 92683

EXAMINER	
GAKH, YELENA G	
ART UNIT	**PAPER NUMBER**
1797	

MAIL DATE	DELIVERY MODE
03/27/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/675,765	NGUYEN ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-60* is/are pending in the application.

4a) Of the above claim(s) *46-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/30/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed on 08/17/07 is acknowledged. The amendment restores the originally filed specification; new claims 31-60 are pending in the application.

Restriction requirement was imposed on the claims in the Office action issued on 04/02/07. Since the new pending claims are basically copies of the originally filed claims, the same requirement is applied to Group I, claims 31-45 and Group II, claims 46-60. In communication with the examiner on 03/10/08 the Applicants elected group I, claims 31-45. Claims 46-60 are withdrawn from consideration. Claims 31-45 are considered on merits.

Information Disclosure Statement

2. The information disclosure statement filed 09/30/03 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

3. Claim 33 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim recites the structural formulas of all possible primary, secondary and tertiary alcohols, and therefore do not further limit the subject matter of the parent claims.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 31-34, 37-40 and 42-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of *quantification* of known alcohols in the sample, does not reasonably provide enablement for the method for *identification* of unknown alcohols in the sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Claim 31 recites the "method of identification and quantification of alcohols", which comprises combining a known amount of an ester internal standard and converting alcohol in the sample into the ester of identical structure to that of the internal standard except for stable isotope atoms. There is no way for a practitioner in the art to take an internal standard, which would differ from an unknown alcohol only by the isotope composition, since the molecular structure of the internal standard would not be known. Moreover, the quantification of the known alcohols can be performed only if there are no losses of the internal standard during synthetic and extracting procedures, since otherwise the amount of the internal standard becomes unknown, which prevents a routineer in the art from quantification of the analyte alcohols.

Claims 35-36 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of *identification* of known alcohols in the sample, does not reasonably provide enablement for the method for *quantification* of unknown alcohols in the sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. There is no way for a routineer in the art to take "a known amount of an ester internal standard", if the internal standard is obtained by the reaction of the sample under analysis, since the amount of the alcohol, which is a starting material for the internal standard is not known in the sample and it is the value to be determined. Moreover, internal standards are used for quantitative determination of analytes, rather than their qualitative analysis. Therefore, utilizing internal standards prepared on the basis of unknown amounts of the analyte, i.e. obtaining internal standards in unknown amounts does not seem to have any practical application, since they cannot be used as real internal standards.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 31-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 recites the "method of identification and quantification of alcohols", which comprises combining a known amount of an ester internal standard and converting alcohol in the sample into the ester of identical structure except for stable isotope atoms. The recitation is unclear and indefinite, since it is not apparent, as to how the first step can be performed with the internal standard, the structure of which is unknown.

Claim 35 recites synthesizing internal standard by reacting an authentic sample of the alcohol with a stable isotope labeled reagent, which makes it unclear as to how the compound obtained from unknown amount of the reagent can be called "internal standard", the amount of which by definition should be known.

Claim 42 recites negative limitation, which is not clear and definite. It is not apparent, as to whether the recitation is referring to labeling the internal standard in specific locations, or it is referring to something else.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. **Claims 31-34, 37-40 and 42-45** are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson (J. Mass Spectrom., 2001) in view of any of Esteban et al. (Anal. Chem., 1987) (Esteban), Dufour et al. (J. Am. Soc. Brew. Chem., 2002) (Dufour) or Pyon et al. (J. Anal. Toxic.,1997).

Johnson teaches "analysis of alcohols, as dimethylglycyrine esters, by electrospray ionization tandem mass spectrometry". He particularly indicates: "[D]imethylglycine (DMG) esters are new derivatives for the rapid, sensitive and selective analysis of primary and secondary alcohols, in complex mixtures, by electrospray ionization tandem mass spectrometry (ESIMS/MS). Their development was inspired by the use of the complementary dimethylaminoethyl esters for the trace, rapid analysis of fatty acids. DMG esters are simply prepared by heating a dichloromethane solution of the imidazolide of dimethylglycine, containing triethylamine, and an alcohol. DMG esters of long-chain fatty alcohols, isoprenoidal alcohols and hydroxy-acids are analysed by electrospray ionization tandem mass spectrometry with a precursor ion of *m/z* 104 scan. Diols, glyceryl esters, glyceryl ethers and some sterols are analysed by a neutral loss of 103 Da scan. Trimethylglycine (TMG) ester iodides, prepared by alkylation of DMG esters with methyl iodide, are more sensitive derivatives for molecules containing secondary alcohol groups, such as cholesterol and gibberellic acid. They are analyzed by a precursor ion of *m/z* 118 scan. DMG or TMG derivatives were shown to be at least comparable and sometimes an order of magnitude more sensitive than *N*-methylpyridyl ether derivatives for ESI-MS/MS analysis of the different classes of alcohols. Applications of these derivatives for the diagnosis of inherited disorders and the analysis of natural products are presented" (Abstract). Johnson also discloses

preparation of dimethylglycine esters via the acid chloride (page 278, right column). Johnson further indicates that "deuterated internal standards labeled in these positions [C-1, C-2 or the terminal carbon] can be used for the quantitation of alcohols" (page 279, right column).

Johnson does not specifically disclose applying isotopically-labeled internal standards of the same structure as the alcohols, which are conventionally used in isotope dilution mass spectrometric method, as disclosed by any of Esteban, Dufour or Pyon.

Esteban teaches "stable isotope dilution thermospray liquid chromatography/mass spectrometry method for determination of sugars and sugar alcohols in humans" (Title); in particular, the method comprises monitoring glucose quantity using D[$^{13}C_6$]glucose as an internal standard.

Dufour teaches "quantitative analysis of beer aromatic alcohols using stable isotope dilution assay", in particular the following: "a quantitative assay of beer aromatic alcohols was developed using gas chromatography (GC) in conjunction with stable isotope dilution analytical (SIDA). Quantification using SIDA is not subject to instrumental and/or sample manipulation variation as any analytical variation has a similar effect on the aromatic alcohols and their corresponding labeled analogs used as internal standard. A range of beers (larger and ale) was spiked with known amounts of deuterated aromatic alcohols, followed by extraction using Et acetate. The beer aromatic alcohols were quantified by GC-mass spectrometry using the corresponding deuterated aromatic alcohols as internal standards. The method was found to be highly repeatable and accurate for the quantification of aromatic alcohols in beer and was far less time-consuming than the conventional method. The aromatic alcohol data for various commercial lagers and ales was statistically analyzed using discriminant function analysis. With few exceptions, the results demonstrated that lagers and ales cannot be distinguished on the basis of the level of aromatic alcohols they contain" (Abstract).

Pyon teaches "An isotope-dilution gas chromatography-mass spectrometry method for trace analysis of xylene metabolites in tissues", in particular the following: "a gas chromatography-mass spectrometry (GC-MS) method using isotope dilution was developed to measure trace levels of xylene metabolites in brain tissues. The primary metabolites of xylene were dimethyl-phenol (DMP), methylbenzyl alcohol (MBA), toluic acid (TA), and methylhippuric acid (MHA). The internal standard was a mixture of deuterated DMP-d3, TA-d7, and MHA-d7.

DMP-d3 was com. available and was used as the internal standard for both DMP and MBA. TA-d7 and MHA-d7 were biosynthesized by administering xylene-d10 to rats and collecting their urine. Based on the noise peaks in 10 blank samples, the on-column limits of quantitation (mean + 10 SD of noise peaks) were approximately 305, 1220, 545, and 386 pg for DMP, MBA, TA, and MHA, respectively. Analyte detection and recovery tests from brain tissues of control rats were conducted by spiking the tissues with 32 nmol/g of each analyte, together with the deuterated metabolites. The tissues were homogenized, extracted with Et acetate, and derivatized by trimethylsilylation" (Abstract). Pyon also indicates that "an advantage to this method is that any loss of the analyte that is due to its chemical behavior during the analysis is corrected relative to the internal standard. Because it is so advantageous to use the deuterated analogue of the analyte as the internal standard, it is beneficial to synthesize the deuterated analogue if it is unavailable commercially" (page 364, left column).

It would have been obvious for a person of ordinary skill in the art to modify Johnson's method by utilizing internal standards prepared from isotopically labeled analytes, as taught by Esteban, Dufour or Pyon for isotope dilution mass spectrometry, because Pyon clearly indicates, "an advantage to this method is that any loss of the analyte that is due to its chemical behavior during the analysis is corrected relative to the internal standard. Because it is so advantageous to use the deuterated analogue of the analyte as the internal standard, it is beneficial to synthesize the deuterated analogue if it is unavailable commercially".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

3/10/2008